



wherein:

$R_1$  is hydrogen, hydroxy,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy, halo, trifluoromethyl, or CN;

$R_2$  is hydrogen ;

$R_3$ ,  $R_4$ , and  $R_5$  independently are hydrogen, hydroxy, halo, trifluoromethyl,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy, nitro, CN, or  $-(O \text{ or } NH)_m-(CH_2)_n-R_9$ , where  $R_9$  is hydrogen, hydroxy,  $COOH$ , or  $NR_{10}R_{11}$ ;

$n$  is 0-4;

$m$  is 0 or 1;

$R_{10}$  and  $R_{11}$  independently are hydrogen or  $C_1$ - $C_8$  alkyl, or taken together with the nitrogen to which they are attached can complete a 3-10 member cyclic ring optionally containing 1, 2, or 3 additional heteroatoms selected from O, S, NH, or N- $C_1$ - $C_8$  alkyl;

$Z$  is  $COOR_7$ , tetrazolyl,  $CONR_6R_7$ ,  $CONHNR_{10}R_{11}$ , or  $CH_2OR_7$ ;

$R_6$  and  $R_7$  independently are hydrogen,  $C_1$ - $C_8$  alkyl,  $C_2$ - $C_8$  alkenyl,  $C_2$ - $C_8$  alkynyl,  $(CO)$ - $C_1$ - $C_8$  alkyl, aryl, heteroaryl, or  $C_3$ - $C_{10}$  cycloalkyl optionally containing one, two, or three heteroatoms selected from O, S, NH, or N alkyl; or  $R_6$  and  $R_7$  together with the nitrogen to which they are attached complete a 3-10 member cyclic ring optionally containing 1, 2, or 3 additional heteroatoms selected from O, S, NH, or N alkyl; and wherein any of the foregoing alkyl, alkenyl, aryl, heterocyclic, and alkynyl groups can be unsubstituted or substituted by halo, hydroxy,  $C_1$ -

C<sub>6</sub> alkoxy, amino, nitro, C<sub>1</sub>-C<sub>4</sub> alkylamino, di(C<sub>1</sub>-C<sub>4</sub>) alkylamino, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, phenyl, phenoxy, C<sub>3</sub>-C<sub>5</sub> heteroaryl, or C<sub>3</sub>-C<sub>5</sub> heteroaryloxy;

or a pharmaceutically acceptable salt, ester, amide, or prodrug thereof.

8. (Once Amended) The method of claim 6, wherein the MEK inhibitor is a compound of Formula (I) wherein (a) R<sub>1</sub> is hydrogen, methyl, methoxy, fluoro, chloro, or bromo; (b) R<sub>2</sub> is hydrogen; (c) R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> independently are hydrogen, fluoro, chloro, bromo, iodo, methyl, methoxy, or nitro; (d) R<sub>10</sub> and R<sub>11</sub> independently are hydrogen or methyl; (e) Z is COOR<sub>7</sub>, tetrazolyl, CONR<sub>6</sub>R<sub>7</sub>, CONHNR<sub>10</sub>R<sub>11</sub>, or CH<sub>2</sub>OR<sub>7</sub>; R<sub>6</sub> and R<sub>7</sub> independently are hydrogen, C<sub>1-4</sub> alkyl, heteroaryl, or C<sub>3-5</sub> cycloalkyl optionally containing one or two heteroatoms selected from O, S, or NH; or R<sub>6</sub> and R<sub>7</sub> together with the nitrogen to which they are attached complete a 5-6 member cyclic ring optionally containing 1 or 2 additional heteroatoms selected from O, NH or N-alkyl; and wherein any of the foregoing alkyl or aryl groups can be unsubstituted or substituted by halo, hydroxy, methoxy, ethoxy, or heteroaryloxy.

14. (Once Amended) The method of claim 1, comprising a MEK inhibitor having a structure selected from:

2- (2-chloro-4-iodophenylamino)-5-chloro-N-cyclopropylmethoxy-3,4-difluorobenzamide;  
 2- (4-iodophenylamino)-N- cyclopropylmethoxy-5-chloro-3,4-difluorobenzamide;  
 2- (4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;  
 2- (2-chloro-4-iodophenylamino)-5-chloro-3,4-difluorobenzoic acid;  
 5-chloro-3,4-difluoro-2- (4-iodo-2-methylphenylamino)- benzoic acid; and  
 5-chloro-N-cyclopropylmethoxy-3,4- difluoro-2- (4-iodo-2-methylphenylamino)-benzamide.

15. (Once Amended) A method of treating or preventing arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the

step of administering an effective antiarthritic amount of a compound selected from:

- A 4  
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- Sub B1  
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- 2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-hydroxy-3,4-difluoro- 5-bromobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluoro-5-bromobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-cyclobutylmethoxy- 3,4-difluoro-5-bromobenzamide;
  - 2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluoro-5-bromobenzamide;
  - 2- (2-Chloro-4-iodophenylamino)-N-hydroxy-3,4-difluoro- 5-bromobenzamide;
  - 2- (2-Chloro-4-iodophenylamino)-N-cyclobutylmethoxy- 3,4-difluorobenzamide;
  - 2-(2-Chloro-4-iodophenylamino)-N-hydroxy-4-fluorobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-hydroxy- 3,4-difluorobenzamide;
  - 2- (2-Methyl-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4,5-trifluorobenzamide; and
  - 2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 4-fluorobenzamide.

16. (Once Amended) The method of Claim 15 wherein said compound is selected from

- 2- (2-chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide;
- 2- (2-Methyl-4-iodophenylamino)-N- cyclopropylmethoxy-3,4,5-trifluorobenzamide; and
- 2- (2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy-4-fluorobenzamide.

Please add following new Claims 17, 18, and 19 as follows:

A 5

Sub  
B  
Cont

17. (New) A method of treating or preventing arthritis in a patient in need of treatment, or suspected of developing arthritis, said method comprising the step of administering an effective antiarthritic amount of 2-(2-Chloro-4-iodophenylamino)-N-cyclopropylmethoxy- 3,4-difluorobenzamide.
18. (New) The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR<sub>7</sub>; R<sub>7</sub> is H, pentafluorophenyl, or tetrazolyl; and R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> are independently H, fluoro, or chloro.
19. (New) The method of Claim 8, wherein the MEK inhibitor is a compound of Formula (I) wherein: Z is COOR<sub>7</sub>; R<sub>7</sub> is H, pentafluorophenyl, or tetrazolyl; and R<sub>3</sub>, R<sub>4</sub>, and R<sub>5</sub> independently are fluoro.